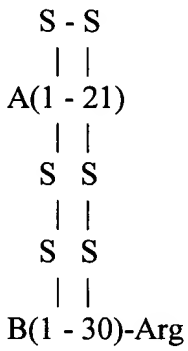
Accompanying this response is a Petition for a Three-Month Extension of Time and the required fee. Kindly enter the following amendment:

IN THE CLAIMS:

Please amend the claims as follows:

21. (Three times amended) A method for the preparation of a mono-Arg-insulin compound of formula II



(II)

in which A(1-21) and B(1-30) denote the A and B chains of human insulin and the -S-S- bridges are positioned as in insulin, which comprises:

(a) expressing as part of a fusion protein in a bacterium a DNA molecule encoding a mini-proinsulin compound of the formula:

B(1-30)-Arg-A(1-21),

(b) liberating said mini-proinsulin compound from said fusion protein;

(c) folding and forming disulfide bridges in said mini-proinsulin compound; [and]

(d) incubating said mini-proinsulin compound with trypsin at a pH of about 6.8 to produce mono-Arg-insulin, under conditions where no crystals are formed; followed by

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(e) precipitating the mono-Arg-insulin.

22. (Three times amended) A method for the preparation of insulin which comprises:

(a) expressing as part of a fusion protein in a bacterium a DNA molecule encoding a mini-proinsulin compound of the formula:

B(1-30)-Arg-A(1-21),

in which B(1-30) and A(1-21) denote the B and A chains of insulin;

(b) liberating said mini-proinsulin compound from said fusion protein;

(c) folding and forming disulfide bridges in said mini-proinsulin compound; [and]

(d) simultaneously incubating said mini-proinsulin compound with trypsin and carboxypeptidase B at a pH of about 6.8 to produce insulin, under conditions where no crystals are formed; followed by

(e) precipitating the insulin.

25. (Three times amended) A method for the preparation of a mono-Arg-insulin compound of formula II

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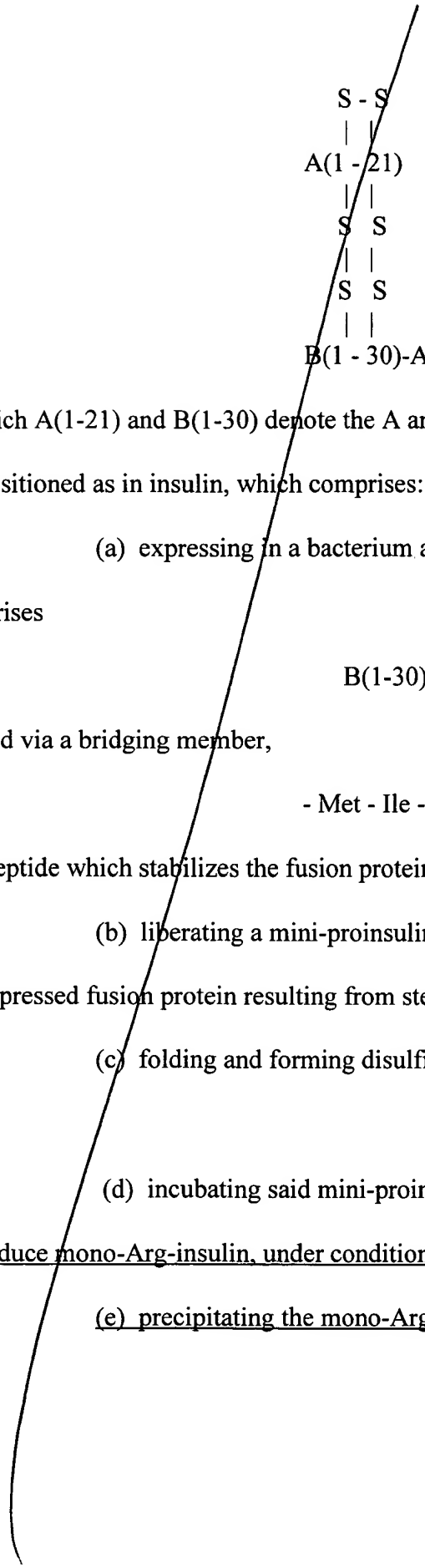

(II)

in which A(1-21) and B(1-30) denote the A and B chains of human insulin and the -S-S- bridges are positioned as in insulin, which comprises:

(a) expressing in a bacterium a DNA molecule encoding a fusion protein which comprises

B(1-30)-Arg-A(1-21)

bonded via a bridging member,

- Met - Ile - Glu - Gly -Arg -,

to a peptide which stabilizes the fusion protein;

(b) liberating a mini-proinsulin compound from said fusion protein by cleaving the expressed fusion protein resulting from step (a) with cyanogen bromide;

(c) folding and forming disulfide bridges in said mini-proinsulin compound; [and]

(d) incubating said mini-proinsulin compound with trypsin at a pH of about 6.8 to produce mono-Arg-insulin, under conditions where no crystals are formed; followed by

(e) precipitating the mono-Arg-insulin.

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26. (Three times amended) A method for the preparation of insulin which comprises:

(a) expressing in a bacterium a DNA molecule encoding a fusion protein which comprises

B(1-30)-Arg-A(1-21)

bonded via a bridging member,

- Met - Ile - Glu - Gly -Arg -,

to a peptide which stabilizes the fusion protein;

(b) liberating a mini-proinsulin compound from said fusion protein by cleaving the expressed fusion protein resulting from step (a) with cyanogen bromide;

(c) folding and forming disulfide bridges in said mini-proinsulin compound;

[and]

(d) simultaneously incubating said mini-proinsulin compound with trypsin and carboxypeptidase B at a pH of about 6.8 to produce insulin, under conditions where no crystals are formed; followed by

(e) precipitating the insulin.

Please add the following new claim:

--31. A method for the preparation of insulin, without formation of substantial amounts of insulin Des-B30, comprising:

(a) expressing in a bacterium a DNA molecule encoding a fusion protein which comprises

B(1-30) - Arg - A(1-21)

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